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Atty. Dkt. No.: 025098-0701

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Peter B. Dervan et al.

Title: DESIGN, SYNTHESIS AND USE
OF SPECIFIC POLYAMIDE DNA-
BINDING LIGANDS

Appl. No.: 09/372,474

Filing Date: 08-11-1999

Examiner: MARSCHEL

Art Unit: 1631

CERTIFICATE OF MAILING I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date below. <u>DIANE GARCIA</u> (Printed Name) <u>Diane Garcia</u> (Signature) <u>7-11-01</u> (Date of Deposit)

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**TRANSMITTAL OF MISSING PARTS
OF PATENT APPLICATION**

TECH CENTER 1600, 1999

Commissioner for Patents
BOX MISSING PARTS
Washington, D.C. 20231

Sir:

In response to the Notice of Non-Compliant Amendment mailed on June 22, 2001, in the above-identified application, transmitted herewith are the missing pages needed to complete the filing of the subject patent application.

Enclosed are:

- ☒ [X] Marked up version of replacement paragraphs
- ☒ [X] Copy of Notice of Non-Compliant Amendment
- ☐ [] Other: Petition for Extension of Time.
- ☐ [] Please charge Deposit Account No. 50-0872 in the amount of \$0.00 in payment of surcharge fee (37 C.F.R. § 1.16(e))

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise

improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

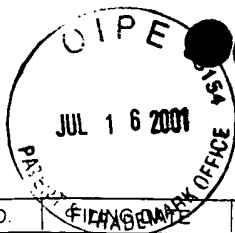
Respectfully submitted,

Date July 11, 2001

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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

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APPLICATION NO.	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/372,474 8/11/99 Baird

EXAMINER

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

DOCKETING DEPARTMENT	
Due:	7/22/01
Drop Date (DD):	
1st Reminder:	6/28/01
Initials:	hwm MDC Entered

025098/0701



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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Notice of Non-Compliant Amendment (37 CFR 1.121)

The amendment filed on 6/14/01 is considered non-compliant because it has not been submitted in the format required under 37 CFR 1.121, as amended on September 8, 2000 (see 65 Fed. Reg. 54603, Sept. 8, 2000 and 1238 O.G. 77, Sept. 19, 2000).

- ☐ The amendment does not include a clean version of the replacement paragraph/section. 37 CFR 1.121(b)(1)(ii)
- ☒ The amendment does not include a marked-up version of the replacement paragraph/section 37 CFR 1.121(b)(1)(iii)
- ☐ The amendment does not include a clean version of the amended claim(s). 37 CFR 1.121(c)(1)(i)
- ☐ The amendment does not include a marked-up version of the amended claim(s). 37 CFR 1.121(c)(1)(ii)

For your convenience, attached to this correspondence is a copy of an informational flyer (MPEP Bookmark Bulletin on "Simplified Amendment Practice").

Applicant is given a TIME PERIOD of ONE (1) MONTH or THIRTY (30) DAYS from the mailing date of this notice, whichever is longer, within which to submit an amendment in compliance with 37 CFR 1.121, effective March 1, 2001, in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 C.F.R. 1.136(a).

Linda Plunkett
Legal Representative



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Description of the Related Art

The design of synthetic ligands that read the information stored in the DNA double helix has been a long standing goal of chemistry. Cell-permeable small molecules which target predetermined DNA sequences are useful for the regulation of gene-expression. Oligodeoxynucleotides that recognize the major groove of double-helical DNA via triple-helix formation bind to a broad range of sequences with high affinity and specificity. Although oligonucleotides and their analogs have been shown to interfere with gene expression, the triple helix approach is limited to purine tracks and suffers from poor cellular uptake. The development of pairing rules for minor groove binding polyamides derived from N-methylpyrrole (Py) and N-methylimidazole (Im) amino acids provides another code to control sequence specificity. An Im/Py pair distinguishes G•C from C•G and both of these from A•T or T•A base pairs. Wade, W.S., Mrksich, M. & Dervan, P.B. describes the design of peptides that bind in the minor groove of DNA at 5'-(A,T)G(A,T)C(A,T)-3' sequences by a dimeric side-by-side motif. *J. Am. Chem. Soc.* **114**, 8783-8794 (1992); Mrksich, M. *et al.* describes antiparallel side-by-side motif for sequence specific-recognition in the minor groove of DNA by the designed peptide 1-methylimidazole-2-carboxamidenetropsin. *Proc. Natl. Acad. Sci. USA* **89**, 7586-7590 (1992); Trauger, J.W., Baird, E. E. Dervan, P.B. describes the recognition of DNA by designed ligands at subnanomolar concentrations. *Nature* **382**, 559-561 (1996). A Py/Py pair specifies A•T from G•C but does not distinguish A•T from T•A. Pelton, J.G. & Wemmer, D.E. describes the structural characterization of a 2-1 distamycin A-d(CGCAAATTTGGC) complex by two-dimensional NMR. *Pro. Natl. Acad. Sci. USA* **86**, 5723-5727 (1989); White, S., Baird, E. E. Dervan, P.B. Describes the effect of the A•T/T•A degeneracy of pyrrole-imidazole polyamide recognition in the minor groove of DNA. *Biochemistry* **35**, 12532-12537 (1996);

(SEQ ID NO: 1)

White, S., Baird, E. E. & Dervan, P.B. describes the pairing rules for recognition in the minor groove of DNA by pyrrole-imidazole polyamides. *Chem. & Biol.* 4, 569-578 (1997); White, S., Baird, E. E. & Dervan, P.B. describes the 5'-3' N-C orientation preference for polyamide binding in the minor groove. New methods of designing selective compounds and the resulting specific polyamide binding ligands that are designed to target an identified sequence of double stranded DNA are needed to overcome the A•T/T•A degeneracy of pyrrole-imidazole polyamide recognition.